EcosistemaIntestinal Viernes 6 Octubre 2017

Su relación con la Patología Inflamatoria Autoinmune

Temas de Fronteras como el Manejo de EII en pacientes con Cáncer, Embarazos, y de la terecera edad.

Asimismo, diagnóstico,manejo medico y quirúrgico de las Fistulas anorectales y sus complicaciones

Finalmente en el dia de hoy se presentarán aquellos trabajos premiados

Un Ecosistema es el medio donde coexisten los seres vivos y no vivientes. Es posible definirlo como un lugar geográfico donde se relacionan los unos con los otros. En el existe una interacción vital, que les permite relacionarse e interactuar entre ellos.

En el caso de la Gastroenterología, el tubo digestivo responde bien a la definición de ecosistema , debido a que es un lugar específico, delimitado por su pared, que no se encuentra vacío , sino que está abierto por sus extremos , por uno de los cuales penetran las bacterias (seres vivos) y los alimentos(seres inertes), los cuales se asocian a las secreciones o substratos digestivos del hospedador(saliva, jugo biliar, jugo pancreático, entre otros).

La luz del tracto gastrointestinal es un reservorio con una superficie interna de aproximadamente 200 mt2 , 100 veces la superficie de la piel. El concepto de ecosistema intestinal surge en la década de los años sesenta (Dubos R, Schaedler RW. The digestión tract as an ecosystem . Amer J Med Sci 1964; 248: 267-271); el cual es regulado por la regulación cualitativa de la microbiota intestinal y las interacciones a que esta sometida la misma con las bacterias entre sí, los sustratos digestivos y el sistema inmunitario.

Previamente se había generalizado el criiterio que el tracto gastrointestinal y los microorganismos contenidos en su interior constituian una unidad ecológica cuyo metabolismo y funciones repercutían en el hospedador , formada por cuatro componentes :

1.- la pared intestinal y la luz de su cavidad

2.- Las secreciones gastrointestinales

3.- La microbiota que habita en el intestino

4.- Los alimentos ingeridos que llegan al interior de su tracto.

Todos los constituyentes de esta Unidad resultan importantes y se interrelacionan entre sí, pues si hay algún cambio de trascendencia en alguno de ellos , los otros componentes resultarían afectados.(Luckey TD The villous in chemostat man. Amer J Clin Nutr 1974 ; 27: 1266-76.)

en el ecosistema intestinal, la composición de la microbiota, caracterizada por su variada multiplicidad. Las limitaciones de los métodos convencionales de estudio , basados en el cultivo microbiano, han aportado una pobre imagen acerca de la biodiversidad de la microbiota intestinal, debido a que la mayoría de las especies bacteriana no han podido ser cultivadas (Suau A; Direct Analysis of genes encoding 16SrRNA from complex communities reveals many molecular species within the human gut. Appl Environ Microbiol 1999; 65.4799-807).

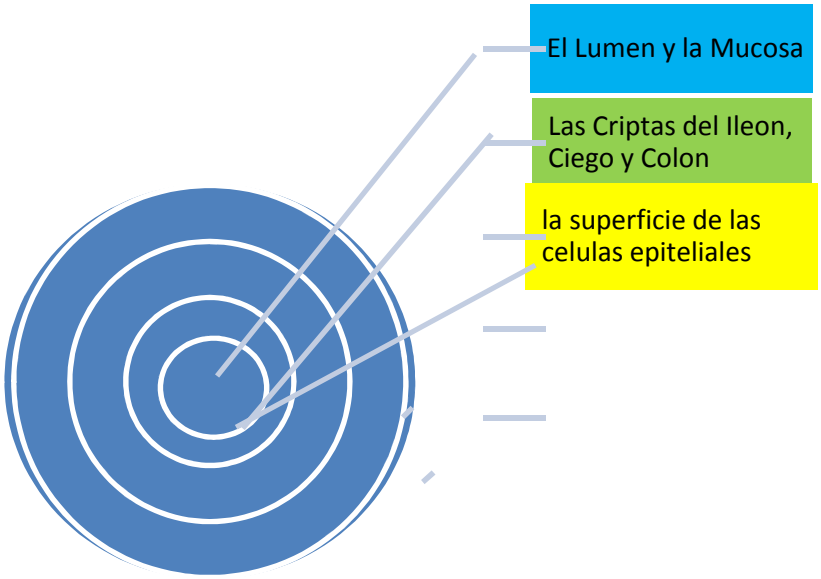
La micro biota intestinal normal, autóctona, endógena , fisiológica esta constituida por las especies presentes de manera constante y con un gradiente de crecimiento progresivo en el sentido buco-anal, capaz de multiplicarse sin producir daño.

Esta microbiota varía según el segmento intestinal, manteniendo su equilibrio asociado a una serie de características beneficiosas, constituyendo un verdadero cultivo autoregulable.

El ecosistema intestinal por su diversidad juega un rol decisivo en las interacciones de la microbiota, con el epitelio de la mucosa intestinal y los mecanismos inmunitarios locales , representado por un equilibrio fisiológico , con la producción de respuestas que se adapatan alos factores agresivos de su medio ambiente(Castañeda C. Ecosistema Intestinal . En: Velasco C. Ed Enfermedades digestivas en el niño . 2da ed Colombia , Universidad del Valle . 2006 , P 27-38.

Esta relación INMUNIDAD INTESTINAL-ECOSISTEMA, están dirigidos a mantener la homeostasis del intestino , la cual se expresa por diversos mecanismos inmunorreguladores, con el objeto de suprimir la respuesta inmunitaria contra los antígenos extraños ; pudiendo ser antígenos de la alimentación , componentes de la microbiota comensalo antígenos asociados con microbios patógenos; unidos a las manifestaciones de tolerancia desempeñada hacia los propios antígenos de la dieta y al microbioma(Iweala OI, Immune previlege in the gut: the establishment and maintenance of non responsiveness to dietary antigens and comensal flora . Immunol Rev 2006; 213:82-100.

El intestino humano es muy complejo en consideración al número de géneros bacterianos o de especies que existen en su interior. Es conocido que ***“el tracto gastrointestinal tiene la más abundante y diversa población de bacterias del cuerpo humano”.*** *Es fundamental para la Microbiota Intestinal se han establecidos cuatro hábitats.*



Muchos microorganismos indígenas o patógenos se unen a la superficie epitelial , mediadas por organelos especiales como las fimbrias(Schrezenmeir J Probióticos, Prebióticos y Simbióticos –Appoaching a definition ¿ Amer J Clin Nutr, 2001; 73(suppl): 361S-4S).

La capa de moco ha sido considerada como hábitat por su acción de protección de hospedador . Las bacterias del lumen dependen de la velocidad del tránsito intestinal

Microbioma y la Microbiota Intestinal

La microbiota humana se estima entre 500 a 1000 especies; y al menos el 50% de las mismas no ha sido cultivada in vivo. Se asume que el tamaño del genoma microbiano contiene como promedio 5 millones de pares de bases y 4000 genes por Genoma.

El "Microbioma del Intestino" contiene de 2.5 a 5 billones de pares de bases y entre 2 y 4 millones de genes , sobrepasando en 140 veces al Genoma Humano

(Hooper LV, Commensal host-bacteria l relationship s in the gut .Science 2001 ; 292: 1115-8).

Los microorganismos y que habitan en el intestino y que constituyen la "microbiota intestinal", ayudan al humano a digerir y absorver los nutrientes como vitaminas, azíucares, fibras entre otros..

El mayor número de estos microorganismos se encuentran en el colon.

Hoy es posible admitir argumentos sólidos que fundamentan la predominancia de las bacterias.

Existen cuatro phylas o divisiones bacterianas:

FIRMICUTES(GRAM POSITIVOS)

BACTERIODETES(GRAM NEGATIVOS)

ACTINOBACTERIAS(GRAM POSITIVAS)

Y PROTEOBACTERIAS(GRAM NEGATIVOS)

También pueden ser residentes , los HONGOS; y ARCHAEA

El avance con nuevos conocimientos adquiridos en el campo de la metagenómica, nos permitirá valorar el el efecto de la edad, la dieta, y determinados estados patológicos, como las EOSINOFILIAS; ENFERMEDADES INFLAMATORIAS INTESTINALES , COMO LA COLITIS ULCEROSA Y CROHN; EL CANCER; y hasta la OBESIDAD en el Microbioma del colon de los humanos en diferentes entornos y como los elementos microbianos del intestino contribuyen a la salud o la enfermedad(Gill SR, Metagenomic analysis of the human distal.

gut microbioma. Science 2006; 312:1355-59); (Peterson DA. Metagenomic approaches for defining the pathogenesids of IBD. Cell Host versus MICROBE. . 2008; 3; 417-26.) (Bibiloni R Microbiota Intestinal, obesidad y Diabetes. Ann Nestlé (ESP) 2009; 67: 39-48).

La interpretación de los eventos que acontecen en el ecosistema intestinal no sólo corresponden a los llamados elementos vivientes o bióticos , es decir la microbiotaintestinal, sino también a una serie de de aspectos relacionados con su medio como:

pH

Grado de Anaerobiosis

Acidos Biliares

Enzimas Pancreáticas

Disponibilidad del Sustrato Endógeno o Exógeno de Origen Alimentario

Sitios de Adherencia Potencial de Microorganismos al Epitelio Mucosal.

EL MOCO(MUCINA)

Y LA VELOCIDAD DEL TRANSITO INTESTINAL.

Estos elementos ya señalados , han sido señalados también como Abióticos, los mismos no son estables con la edad, ni en las diferentes secciones del intestino, lo que le entrega originalidad an los rasgos del ECOSISTEMA INTESTINAL(Hagiage"La

Flore Intestinale del' Equilibre au desequilibre" "Ecosysteme Intestinal ED Vigot, France 1994 p 31-46.

De lo anterior podemos postular que el ecosistema intestinal puede ser modificado por elementos vivientes y no vivientes(bióticos y abióticos).

Esta modulación se puede producir en cualquier edad de la vid; y son exponentes de la misma , los elementos bióticos, representados por los probióticos, por su efecto preventivo y curativo. Así como los abióticos, como las fibras alimentarias y los almidones resistentes a los prebióticos (Marteau. Fcteurs de controle de la flore. Definitioes et mode de action des probiotiques et prebiotiquesen : FLORE MICROBIENNE INTESTINALE. París John Libbey Eurotext, 2004: p 37-58..

El conocimiento de la Complejidad del Intestino humanao, resulta un real ejemplo del significado de su ecosistema.

<u>PRINCIPALES TECNICAS USADAS Y FUNDAMENTOS CON SUS VENTAJAS Y LIMITACIONES</u>

(BLAUT M. Molecular Biological Methods for Studying THE GUT MICROBIOTA: The EU Human GUT FLORA PROJECT. BRIT J NUTR 2002; 87(Suppl 2) ; S203-11).

Nombre Tecnica	***Fundamento***	***Caracteristicas***
Hibridización Fluorescente in situ uorg en espacio	***Una sonda de Oligonucleotidos Fluorescente para secuencia ARN***	***Para ver***
PCR-EGGD/RCP-EGGT POBLS	***EGGD/EGGT EXTRACCION AND ARNr165ampliadoporPCR***	***DETECTAR DOMINANTE(1% POBLBACT)***
PCR CUANT TIEMPOREAL REALESPECIF(+)SENSIBILID	***AMPLIF ADN/ARNCON SONDAS OLIGONUCL. FLUORESCENTES***	***T***

<u>TEMAS ENFERMEDAD INFLAMATORIA INTESTINAL DE FRONTERA BERLÏN OCTUBRE 2017</u>

1.- Manejo de la EII en pacientes de Edad

Guillaume Savoye MD PhD (Lynch 2010, British Audit 2008-2010. Pstoperative Complications

PROFF GASTROENTEROLOGY , NORMANDY UNIVERSITY ROUEN UNIVERSITY HOSPITAL. RUEN FRANCE.

De acuerdo a la edad la población Occidental, en los ancianos, el tema EII, permanence y aún más aumenta progresivamente.

El diagnóstico y manejo de la Colitis Ulcerosa y Enfermedad de Crohn, resulta todo un desafío. Primero, porque el diagnóstico de EII en un adulto mayor no se piensa tan fácilmente como en un paciente joven. De esta manera, una vez que el diagnóstico ya ha sido confirmado en pacientes de esta edad; se debe pensar en las comorbilidades , como el Clostridium Difficile, Eventos venosos tromboembólicos con hospitalizaciones;

Los estudios, de terapia demuestran altas dosis de Corticoides y de aminosalicilatos, con bajos niveles de usos de inmunomoduladores y de uso biológico. Cuidado con el DOCETAXAL; Y SORAFINIB)

Sin embargo, algunos de estos pacientes de la tercera edad, requieren urgente inmunomoduladores y tratamiento con salicilatos

2. Otras Entidades como el descubrir Cancer(LAURENT BEAUGIERE)del DptoGastroenterology Hospital Saint Antoine Paris France; permite elegir el tratamiento oncológico más adecuado, siguiendo los Protocolos oncológicos.

No hay estudios que señalen una incidencia de mayor número de cáncer

Los pacientes con antecedente de haber presentado cáncer, presentan un alto riesgo de un segundo Cáncer(overall de 14% que es un alto riesgo ; versus el 1.9 (1.3 a 3.0) en pacientes habituales .

En este contexto clínico, los pacientes con cáncer previo y EII, aumentan exponencialmente su riesgo a un nuevo cáncer.

Shelton (Gastroenterology 2016)

Habla del BUT 1 y BUT 2.

En el caso de BUT 1, la práctica clínica diaria, el uso de terapia inmunosupresora, aumenta el riesgo de una recurrencia oncológica.

BUT 2; No aumenta significativamente esta incidencia en el inmunoseguimiento

Sosa nat Rev Cancer 2014; 14: 6 11.

Es justamente en esta etapa del inmunoseguimiento, se puede activar la citotoxicidda de los Linfocitos T natural Killer .

Sobrevidas prolongadas en estadio tres , obligan a los familiares con pacientes en etapa tres ; como los melanomas, ajustar la dosis de fármacos como el Infliximab, ajustando la dosis inicial

A continuación se expondrán los principales posters que tuvieron un impacto particular

Queda por evaluar algunos temas de frontera como:

Cerrar las fistulas con tejido adiposo derivado de las células de stem.

Manejo de las Fistulas anorectales; mediante apoyo diagnóstico-imageneológico ej EUS-MRI.

Y terapia médica y quirúrgica de estos pacientes. Y el apoyo real de la terapia biológica, apoyados en los Protocolos que se han creado con el primer mundo, para beneficio de nuestros pacientes.

VIERNES 6 de Octubre 2017

3.-EII Y EMBARAZO:

Prof DR CJ VAN DER o, nes bmWOUDE

Señala que en su Universidad el cuadro clínico .

Se asocia más a cuadros de riesgo de aborto en el segundo trimestre (de Lima A AM J Gastroenterology 2016).

Se recomienda:

1. ***Evaluar los riesgos de un embarazo previo a embarazarse***
2. ***Tratar en lo posible por no embarazarse***
3. ***Tratar inmediatamente diagnosticado la EII, independiente del tiempo de gestación***
4. ***Si es posible, limitar lo mas posible, la exposición del bebé alas drogas***
5. ***Recordar que durante el segundo semestre, habitualmente la EII se detiene***
6. ***En general, las drogas biológicamente activas tienen un bajo incidencia de alteraciones en la fertilidad, abortos, como teratogénesis. Ej MESALAZINA, CORTICOIDES ANTITNFALFA; Thiopurinas .***
7. ***Menos conocidas pero en aquellos que se les ha dado, la incidencia de aborto y teratogenicidad es bajo:***

8. ***USTEKIMUMAB***
9. ***NATALITUMAB***
10. ***VEDOLIZUMABde LIMA GUT 2015 01-8; señala que las thiopurinas podrían suspenderse durante la remisión, la cual suele ocurrir en el transcurso del segundo semestre.***
11. ***Se concluye entonces , que a pesar de lo que se había señalado años antes, la mayoría de las drogas podrían mantenerse***

OTROS TEMAS DE FRONTERAS:

A continuación entregaremos en ingles material obtenido desde el actual Simposio de Berlín. Utilizando como introducción, parte de nuestro trabajo acerca del rol de TH17 in IBD.

Role of Th17 Cells in Inflammatory Bowel Disease "

Semester VII , Clinical Bioanalysis , Hematology and Bank Sangre.-

Authors: Sergio Alberto Carrasco Anabalón. Diego Javier Zapata Tapia. T. M MsC (c) Marcelo Castillo Navarrete. . Fernando Kawaguchi. MD. PhD

Summary.

Thus it has also been found that the prevalence of the disease is increasing.-

Immune Response Bowel and Pathogenesis of disease.-

Basically the immune response of normal bowel is given by three cell types: Paneth cells (CP) whose function is to identify metabolites of gram (+) and muramyl dipeptide through NOD2 / CAR15 called intracellular receptors and induce secretion of various proinflammatory interleukins.

Introduction.-

The term "Inflammatory Bowel Disease" means a group of diseases of the digestive tract that is characterized by chronic inflammatory processes associated with extraintestinal manifestations of various kinds and frequent complications associated with and exaggerated immune response to the constituents of the mucosa and components the luminal flora individuals with a genetic predisposition.

Crohn's disease (CD) and Ulcerative Colitis (UC) are the two major forms of inflammatory bowel disease (IBD) where the development of these will be linked to periods of activity and periods of latency. (1) (2)

Formerly it was believed that the two entities named were one but through the years has been both a differential based on the distribution of disease diagnosis, clinical, molecular mediators involved, treatment and prevalence. However generally still it uses the term "inflammatory bowel disease" as a set and are considered of great importance in current clinical because they cause severe deterioration of the quality of life of those who suffer, besides being related to high incidence of colorectal cancer. (3)

As in the other patterns of cytokine expression, there are certain cytokines which may interfere with the development and proliferation of Th17 cells, certain cytokines and well increase their presence particular circumstances. The suppression of Th1 and Th2, IFN-y and IL-4 increases the number of cells producing IL-17, generated by stimulation of IL-23. In turn, IL-27, IL-25 and IL-13 have inhibitory potential TH17 development. The absence of these cytokines exacerbates inflammatory processes and increases the number of TH17 cells in an inflammatory focus. As also seen in the Th1 / Th2 differentiation, the presence of costimulatory molecules CD80, CD86, OX40 and ICOS (15) is essential for TH17 differentiation in the presence of IL-23.

Role of Th17 cells in inflammatory disease Intestinal.-

Local effects of IL-17 are to stimulate the production of IL-6, nitric oxide and prostaglandin E2, also acts at the same synergistically time with other IL proinflammatory as IL-1beta, tumor necrosis factor, IFN-y and CD40 ligand, leading to upregulation of gene expression and amplification of the local inflammatory response. IL-17 has an effect of neutrophil and monocyte chemoattractant to sites of inflammation through mediators like IL-8, monocyte chemoattractant protein (MCP) -1 and growth related protein. At the same time increases

From the immunological point of view the EC was associated with the expression pattern of TH1 and secretion of INF-y, IL-12 and TNF, while the CU with the pattern of expression of Th2 cytokines and secretion of IL-4, IL -5 and IL-13 (4). Plus you're expressing IL-2, IL-21, IL-23 in common. Subsequently described in CD4 + cells the expression pattern of Th17 cytokines, IL-17 production by stimulating IL-23 and associated with the disease. (5)

Then, in subsequent studies we determined the existence of cells with an expression pattern of Th1 / producing Th17 of IFNy, IL-17 and IL-9 recently discovered, which has been described as cytokine effector Th17 cells current theories and the expression of this cytokine is associated with an independent pattern, called Th9.

In inflammatory bowel disease, IL-17, regardless of origin, is found in abundance in inflamed intestinal mucosa. Other autoimmune chronic diseases such as rheumatoid arthritis, multiple sclerosis, systemic sclerosis, systemic lupus erythematosus, asthma, also share the overexpression of IL-17 by Th17 cells.

The treatment of this disease is very expensive, and often ineffective (6). Therefore the study of the mechanisms involved in its pathogenesis is very important and is a priority in order to guide new treatments and diagnostic tools (7). Therefore the study of these mechanisms, especially the immune and given the advances in the knowledge of these are of great importance to contribute and health of those affected.

Epidemiology.-

Its prevalence is higher, especially Western industrialized countries, where it occurs at earlier ages and with different evolution. In northern Europe, the UK and North America an incidence of 6.5 cases per 100,000 people described, with the highest incidence of over 50 years.

Meanwhile in Chile there are no statistically significant data on incidence, but if some authors as clinical experience in these cases denote a bimodal age distribution of cases. The vast majority occurs between 15 and 25 years, so between 55 and 66 years old. (8)

The imbalance of cytokines which would contribute to the constant and inappropriate activation of the immune system in the intestine.

The other type of cells involved are cells M (M differentiated epithelial type) which possess on their surface TLR receptors, mainly type and TLR4 are associated with integrins and PAF release.

The last prominent cell type are dendritic cells (DC), whose function is to link the innate immunity response with acquired through activation of secondary lymphoid organs, thereby leading to the induction of Th1 or Th2 patterns. Found in Mucosal Associated Lymphoid Tissue (malts), mainly in Peyer's patches, mesenteric lymph nodes and in the lamina propria by their pseudópodios where you can catch luminal antigens through small intestinal epithelial intercellular openings (9).

These antigens collected, which generally come from epithelial cells, food or commensal bacteria are presented to T cells Malts under an inducer of a state of inactivation of these cells to generate immune tolerance environment. Also the importance of these CDs is that they can present an anti-inflammatory Th2 pattern. Studies indicate that the development

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Lysozyme also secrete α-B, phospholipase A2 and defensins and other molecules that protect the intestinal epithelium ingested pathogens and also limit the commensal flora. Particularly defensins stimulate the secretion of IL-18 promotes the attraction of lymphocytes to the site of infection, it has been seen in the EC are reduced secretion of these defensins which would favor colonization by pathogenic bacteria (Mycobacterium avium, Campylobacter spp. And Salmonella spp., among others) as well as contribute to

of anti-inflammatory CD various epithelial cells expressing mediators such as TSLP or thymic lymphopoietin stroma involved, which although not interfere with IL-12 (stimulant

pattern Th1) maintains induction predominance of Th2 pattern against antigens bacterial, which is important since it has been shown that expression of TSLP in CD patients is poor, so it is thought that this factor is important in the pathogenesis of CD as well as in the intestinal tolerance (10).

In addition to the components described above, over the years it has been postulated genetic predisposition to the disease. There is evidence of some polymorphisms involved eg NOD2 / CARD15 receptor synthesized by chromosome 16 and is expressed in monocytes, CDs, intestinal epithelium and Paneth cells (CP), these polymorphisms in Crohn's disease are associated with a earlier onset of the disease, ileal location, presence of extensive stenosis and entero-enteric fistulas.

have also been described Polymorphisms as Arg702Trp, Gly908Arg and Leu1007fsinsC that relate to the predisposition to develop as these mutations are related to phagocytic defects level macrophage EC, causing intracellular infections causing constant stimulation of the cells causing an imbalance between effector cells and regulatory. Patients who have these polymorphisms are associated with disease onset earliest. Also described polymorphisms associated to high expression of type TLR4 receptors in patients with CD. In Chile, some patients with IBD have these mutations in NOD2 / CARD17 and TLR4.

Current evidence discloses that there is also a polymorphism of IL-23 receptor, which is believed to provide protection against the development of EC.

All this, supports postulates that IBD are abnormal mucosal inflammatory responses against intestinal commensal flora in individuals with genetic predisposition.

Basically in IBD it described the phenomenon can start with three different inducers mechanisms of inflammation (11) may be an alteration of the epithelial barrier given by a loss in the intercellular junctions which causes a migration of bacterial antigens between cells (1) into the lamina propria, or certain bacteria of the intestinal lumen may trigger an inflammatory process by direct interaction with epithelial TLR (14). And finally mediated phagocytosis dendritic cells are able to reach the lumen through its pseudopódios through intercellular spaces (10). These dendritic cells have lost their tolerogenic properties can stimulate T Lymphocytes Virgin by the transcription factor T-bet and take them to express a pattern of expression of Th1 or Th17 in the case that induction is by IL-23 (11) (12).

In CD, the bacterial antigens are aberrantly presented by macrophages to T Lymphocytes virgin (2), which are induced to express a Th1 cytokine pattern causing secretion of a high concentration of proinflammatory cytokines, including INT-γ that promote the production of IL-12 by the macrophage and is in turn stimulate the T lymphocyte Th1 thereby causing an overstimulation of the secretion of proinflammatory cytokines that act on populations of local cells promoting their death and further recruitment of other cells inflammatory and local tissue destruction.

In turn occurs a defective apoptosis of activated T lymphocytes causing an accumulation of these and increasing the concentration of proinflammatory cytokines (3). IL-17 produced by Th17 Lymphocytes promote neutrophil recruitment into the inflamed gut (13), also IL-8

secreted by stimulation via IL-17 produced by lymphocytes Th17 (12), or by direct interaction with epithelial antigen TLR (14) also contribute to neutrophil recruitment to inflamed intestinal mucosa (13). The greatest damage is given by the release of high concentrations of TNF-α from activated macrophages, which will also promote the recruitment of neutrophils to the gut inflamed by an up-regulation of adhesion molecules in the vascular endothelium of blood vessels the intestinal mucosa which interact with integrins expressed in T-lymphocytes (9).

TNF-α also be responsible for epithelial damage, de-epithelialization of the mucosa and ulceration (5) further promote the production of metalloproteinases (MMPs) matrix fibroblasts that are directly responsible for the degradation of connective tissue and ulceration (6) ultimately leading to fibrosis of the bowel wall. In the case of CD, TNF-α also cause the formation of granulomas (8), imbalance in the fibroblastic secretion into excess tissue inhibitors of metalloproteinases (TIMP) which increase collagen deposition, fibrosis and stenosis (7), and fistulae.

Among the various cytokines studied, it is stated that TGF-β in the presence of stenosis is overexpressed together with their receptors, causing level epithelium alteration in structure characterized by reducing the tight junctions of cell-cell and remodeling was making a fibroblastic- morphology.

Th17 cells, characteristics and its role in the system inmune.-

After production, all virgin T cell must acquire a lineage-specific cytokine expression, whether natural or induced way. In addition to the usual patterns of expression of cytokines such as Th1 and Th2, widely described in the literature, other patterns appear after scientific study, where situations where they do not fit into existing schemes are there. In consideration of this gaze beyond the Th1 / Th2 patterns expanded, being put into debate its unique existence, mainly due to study in murine models, where it was discovered that signaling by IFN-y does not confer the development of autoimmunity, On the contrary, they become more susceptible. the existence of additional subtypes of T cells, which differ from Th1 and would be able to induce and perpetuate a local inflammation and autoimmunity, in this context, come into play Th17 cells, which are a main focus of this work was raised.

Th17 cells studies were initially conducted in animal models infected Borrelia burgdorferi, in which the induction of IL-17 production by T cells independently of production by Th1 and Th2 patterns achieved. Subsequently, the IL-17 pattern was induced by Mycobacterium bovis BCG strain, obtaining similar results. Further evidence that ensures discovery of this cell population comes from studies of autoimmunity in mice with rheumatoid arthritis and multiple sclerosis. The main defining characteristic of this pattern of cytokine expression is associated with the secretion of large amounts of IL-17 and termed Th17.

The IL-17 (also called IL-17A) and IL-17F (13) cytokines, which are secreted into this pattern of cytokines are members of the IL-17 family and in turn, potent inducers of

inflammation, promoting infiltration cell and the production of certain proinflammatory cytokines and chemokines. The wide distribution in tissues and cells of IL-17 receptor, called IL-17R, in humans and mice, explains its importance in the immune response.

With the opening of Th1 / Th2 paradigm, while the TH17 cells, many answers about the pathophysiology of certain chronic can now be better understood diseases discovering, because with existing information from previous form was not possible to give a clear answer and concise. Studies in animal models have demonstrated that neutralization of IL-17, without interfering action of Th1, is able to provide complete recovery in some autoimmune diseases. Also, other recent studies have delivered a key role in Th17 cells in the pathophysiology of inflammatory diseases, including viral hepatitis (14), asthma and transplant rejection.

the production of hematopoietic growth factors such as granulocyte colony stimulating factor (G-CSF) and granulocyte - macrophage (GM) -CSF which promotes the growth and maturation of myeloid cells recruited. Furthermore IL-17 is a bridge between innate and acquired immune response by increasing the induction of costimulatory molecules such as ICAM-1 by other cytokines, thereby holding cell activation T.-

Research in mice, it has been determined that the IRF4 is involved in the development of experimental autoimmune encephalomyelitis and that the deficit IRF4 protects mice from the disease. Studies also indicate that active IRF4 directly to IL-17 A binding by direct promoter. Recently it described the CD161 as a marker surface potential related to the progression of Th17 mediated IBD.

One of the main features of Th17 cells is to secrete IL-17, whose members of this family of cytokine can be expressed by different cell types T-γσ, NK-T cells, NK, T lymphocytes CD8ct cells, neutrophils, eosinophils, fibroblasts, macrophages, etc.

Within the family of IL-17, IL-17A highlights and IL-17F that they are capable of inducing the expression of several proinflammatory cytokine and chemokines in various cells presenting IL-17RA Receptor. Major proinflammatory effects of these cytokines are mediated by TNF-α induction, IL-1β, chemokines (CXCL8, CXCL1, CXCL10) GM-CSF, G-CSF, IL-6, and metalloproteases. These are tested proinflammatory effects on the intestinal epithelium, endothelium osteoblasts and others. The role of IL-17A and IL-17F apart from its effects described is the recruitment, activation and migration of neutrophils, the function differs in IL-17E recruiting eosinophils and basophils. For the latter function expression Th2 with IL-5, IL-14, IL-4 (18) is necessary.

Secretion of IL-17A is not limited to patients with IBD, but high levels of mRNA expression of IL-17A if they will be associated with patients with IBD, so high levels of mRNA expression of IL-17F they will be associated with active CD. Increased levels of expression are favored by stimulation by IL-17 in active CD and UC. It is shown that there is increased production of IL-17 in inflamed mucosa from IBD, but not in non-inflamed mucosa with IBD positive and negative controls (The study was conducted by cell culture biopsy).

In consideration of the above, IL-17A and F will have a very important role pathogen, can manifest even in experimental models of IBD, as is in murine colitis. For example, studies with knockout mice IL-17R (not possess the receptor for IL-17), these were protected for weight loss TNBS-induced, and also for colonic inflammation produced and local induction of inflammatory protein-2 macrophagic, it can be demonstrated that IL-17R signaling is crucial in acute colitis TNBS. Indirectly, this approach is supported by the Th17, major producers of IL-17 cells are at least as efficient and powerful in transfer colitis in knockout mice in Th1 cells RAG. IL-17F-induced colitis exacerbate dextran sodium sulfate, but not in the case of knockout mice IL-17F that are relatively protected.

When considered together, the greater implication of IL-17 A and F in inflammatory bowel disease is the perpetuation of inflammation secondary stimulation of proinflammatory cytokines and chemokines. On the other hand, it has been seen that there is a complex and lattice interaction between Th17 cells and intestinal epithelial cells (IEC), which favor the perpetuation of intestinal inflammation and the CIS secrete IL-17R and receptors for IL-22 and IL -26.

Beyond the stimulation, IL-17 A, also mediates the protective effects inflammatory response in the gut epithelial barrier by modulating tj via claudins and the upregulation of the expression of antimicrobial peptides.

When intestinal epithelial cells are stimulated by cytokines Th17 pattern, these secrete a wide range of proinflammatory cytokines and chemokines such as neutrophil CXCL8 chemotaxis and CCL20 for attraction of Th17 cells and dendritic cells, amplifying intestinal inflammation. Recent studies confer a protective role for IL-17 A in intestinal inflammation, when this is mediated by T cells, but in this sense, there is still controversy and conflicting data. For example Awasthi and Kuchroo showed that IL-17 Inhibits Th1 cells directly and thus suppresses the development of intestinal disease. Ogawa and colleagues reported that treatment with monoclonal anti IL-17 induced colitis to worsen with DSS, being clearly these dichotomous outcomes.